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10/541,657	03/03/2006	Robert M. Jones	34.US5.PCT	4098
26204	7590	07/12/2011	EXAMINER	
FISH & RICHARDSON P.C.			JARRELL, NOBLE E	
P.O. BOX 1022				
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			ART UNIT	PAPER NUMBER
			1622	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No. 10/541,657	Applicant(s) JONES ET AL.
	Examiner NOBLE JARRELL	Art Unit 1622

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 April 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 12-14, 17-66, 73, 74, 79-85, 90-92 and 100-115 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 12-14, 17-66, 73, 74, 79-85, 90-92 and 100-115 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>15 April 2011</u> . | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1622

DETAILED ACTION

Response to Amendment

1. Claims 1-5, 12-14, 17-66, 73, 74, 79-85, 90-92, and 100-115 are pending in the instant application.

Priority

2. The priority date of the instant application is 14 January 2003.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-5, 12-14, 17-66, 73, 74, 79-85, 90-92, and 100-115 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical acceptable salt of a compound of formula (Ia), does not reasonably provide enablement for a hydrate or solvate for a compound of formula (Ia). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Art Unit: 1622

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a compound in which a pyrimidine ring is modified with a NH-C(=NR⁸)NHR⁷ at its 5-position and nitrogen-containing heterocyclic ring at its 4-position.

Thus, the claims taken together with the specification imply that a pharmaceutically acceptable salt, hydrate, or a solvate of these compounds can be prepared.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Hildesheim et al. (US 7056942, issued 6 June 2006) describe that solvate or hydrate formation/existence is unpredictable (column 2, line 60 to column 3, line 14).

(5) The relative skill of those in the art:

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position (MD's, PhD's, or those with advanced degrees and the requisite experience in hydrate or solvate formation).

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for a pharmaceutically acceptable salt of a compound of formula (Ia).

However, the specification does not provide guidance for a solvate or hydrate of a compound of formula (Ia).

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-5, 12-14, 17-66, 73, 74, 79-85, 90-92, and 100-115 and the high unpredictability in the art as

Art Unit: 1622

evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

This rejection is maintained because Hildesheim describes that hydrate or solvate formation is unpredictable. Vlppagunta also points to unpredictability in solvate or hydrate formation (section 3.4, page 18). Due to the presence of these teachings, it appears that solvate or hydrate formation is unpredictable.

5. Claims 79-85, 90-92, and 110-115 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of obesity, type II diabetes, a metabolic syndrome, insulin resistance, inadequate glucose tolerance, hyperglycemia, hypertriglyceridemia, and hypercholesteremia, does not reasonably provide enablement for the prophylaxis of obesity, type II diabetes, a metabolic syndrome, insulin resistance, inadequate glucose tolerance, hyperglycemia, hypertriglyceridemia, and hypercholesteremia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to treatment or prophylaxis of a disease using a compound in which a pyrimidine ring is modified with a $\text{NH-C(=NR}^8\text{)NHR}^7$ at its 5-position and nitrogen-containing heterocyclic ring at its 4-position. Thus, the claims taken together with the specification imply that a disease recited in claims 79-85, 90-92, and 110-115 can be treated or prevented with a compound of claim 1.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Obesity is prevented through diet management, weight monitoring, and exercise.

Obesity is one type of hyperlipidemia and hypertriglyceridemia ("Obesity: Prevention", <http://www.mayoclinic.com/health/obesity/ds00314/dsection=prevention>, accessed 1 July 2011, attached as PDF).

Diabetes type II prevented by losing an appropriate amount of weight. Diabetes type II is one type of a metabolic syndrome, insulin resistance, and inadequate glucose tolerance ("NDEP", <http://ndep.nih.gov/diabetes/prev/prevention.htm>, accessed 1 July 2011, attached as PDF; "Insulin resistance and Pre-Diabetes", <http://diabetes.niddk.nih.gov/dm/pubs/insulinresistance/>, accessed 1 July 2011, attached as PDF).

Hyperglycemia is prevented through weight loss ("High blood sugar", http://www.emedicinehealth.com/high_blood_sugar_hyperglycemia/page9_em.htm, accessed 1 July 2011, attached as PDF).

Art Unit: 1622

Hypercholesterolemia is prevented through diet management ("Familial hypercholesterolemia", <http://www.umm.edu/ency/article/000392prv.htm>, accessed 1 July 2011, attached as PDF).

(5) The relative skill of those in the art:

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position (MD's, PhD's, or those with advanced degrees and the requisite experience in INSERT METHOD HERE).

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for treatment of obesity, type II diabetes, a metabolic syndrome, insulin resistance, inadequate glucose tolerance, hyperglycemia, hypertriglyceridemia, and hypercholesterolemia.

However, the specification does not provide guidance for prophylaxis of obesity, type II diabetes, a metabolic syndrome, insulin resistance, inadequate glucose tolerance, hyperglycemia, hypertriglyceridemia, and hypercholesterolemia.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 79-85, 90-92, and 110-115 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-5, 12-14, 16-66, 73, 74, 78-85, 87-92, 100, and newly added claim 110-115 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 12-14, 17-66, 73, 74, 79-85, 87-92, and 100 of copending Application No. 12/945712 (continuation of 10/541657, filing date of 10 November 2010, priority to 14 January 2003).

Art Unit: 1622

Although the conflicting claims are not identical, they are not patentably distinct from each other because the first recited compounds of claims 73 and 74 of application 10/541657 are encompassed by the specified claims in both applications. In claims 73 of both applications, the first recited compound is the same. The second compound of claim 74 of application 10/541657 is the same compound is the same compound as the fourth compound of claim 74 of application 12/945712.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

This rejection is maintained because the application is not in condition for allowance.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. None of the claims appear free over the prior art of the record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on M-F 8:30 A.M - 5:00 P.M. EST.

Art Unit: 1622

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Andrew D. Kosar can be reached on (571) 272-0913. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Primary Examiner, Art Unit 1622